PATENT COOPERATION TREATY

RECEIVED
2005 -08- 09
U-A PD

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Amersham Biosciences AB
Patent Department
Björkgatan 30
751 84 Uppsala

DEPARTMENT: 7 Oct 2005
FORMALITIES: DP ✓
PAT. OFF: AK ✓
ON DB: 10/8/05
CASE NO: PU0372-PCT

PCT

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 66)

Date of mailing *(day/month/year)*	08 -08- 2005
Applicant's or agent's file reference: PU0372-PCT ✓	REPLY DUE: within 60 days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2004/001414 ✓	05.10.2004	06.10.2003

International Patent Classification (IPC) or both national classification and IPC
C07K 17/00, C12N 5/00, C07C 29/00

Applicant
Amersham Biosciences AB et al

1. ☒ The written opinion established by the International Searching Authority:
   ☒ is ☐ is not
   considered to be a written opinion of the International Preliminary Examining Authority.

2. This second (first, etc.) opinion contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.
   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).
   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.
   Also For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.
   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 06.02.2006

Name and mailing address of the IPEA/SE	Authorized officer
Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 46 8 667 72 88	Malin Söderman/Els Telephone No. 46 8 782 25 00

Form PCT/IPEA/408 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/001414

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☐ the international application in the language in which it was filed

☐ a translation of the international application into _____ ,
which is the language of a translation furnished for the purposes of:

☐ international search (Rules 12.3(a) and 23.1(b))

☐ publication of the international application (Rule 12.4(a))

☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this opinion has been established on the basis of *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."):*

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages _____ as amended (together with any statement) under Article 19
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/001414

Box No. V **Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	
	Claims	
Inventive step (IS)	Claims	
	Claims	1-6, 9-14, 16-30 (NO)
Industrial applicability (IA)	Claims	
	Claims	

2. Citations and explanations:

Reference is made to the following documents:
D1: US6378527 B1
D2: US6103479 A
D3: EP0420171 A1
D4: US2003133988 A1
D5: US5512474 A
D6: WO03072155 A1
D7: US6407208 B1

The invention relates to a microcarrier onto the surface of which a cationic compound has been immobilised via a guanidine group. The microcarrier is capable of attachment of cells, e.g. via charged-based interaction, and is used as a support in the culture of cells. The cationic compound may comprise one or two amino acids, such as arginine or a dipeptide. The invention also relates to a method of preparing a polycationic microcarrier, which method comprises immobilising a compound that comprises at least one guanidine group to an epoxide-activated substrate.

Document D1 is considered to represent the closest prior art. D1 describes methods for cell culture using polymers as microcarriers. The polymers should contain cationic groups to allow cell attachment, see column 12, line 43-column 13, line 21. To add cationic nature to the beads, different groups could be added to the polymer, for instance arginine, see column 16, line 67-column 17, line 7. Dextran, cellulose or another compound could be used as a microcarrier, see columns 15 and 16.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

The invention according to claims 1, 2, 4-6, 10, 11, 19-23 and 25-30 differs from the method in D1 in that it explicitly describes that a cationic compound, for instance arginine, is immobilised to a microcarrier via a guanidine group. D1 does not describe how arginine is bound to the microcarrier.

It is not clear from the claimed invention why it is more advantageous to have a guanidine group than another group. It is not clear from the claimed invention what type of microcarrier is used. Consequently, with the background of D1, the problem is to find a method to attach arginine to a microcarrier.

It is considered obvious to a person skilled in the art to use what is known from D1, where arginine is known to be used as a cationic compound in microcarriers, to create microcarriers described in the claimed invention according to claims 1, 2, 4-6, 10, 11, 19-23 and 25-30. It is considered obvious to a person skilled in the art to attach arginine via a guanidine group to a microcarrier when it is known that arginine could be attached to a microcarrier. Hence, the invention according to claims 1, 2, 4-6, 10, 11, 19-23 and 25-30 is not considered to involve an inventive step.

According to the arguments stated above, the subject matter defined in claims 3 and 9 is considered to relate to measures obvious to a person skilled in the art. Therefore, claims 3 and 9 are not considered to involve an inventive step.

It is known to use cells in high throughput screening (HTS), see D2 abstract. D1 and D2 are considered to relate to the same technical field. Therefore, it is considered obvious to a person skilled in the art to combine D1 and D2 to achieve the claimed invention according to claim 24. Hence, claim 24 is not considered to involve an inventive step.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

Claims 12-14, 17, 18 differ from D1 in that the surface of the substrate is epoxide-activated. D3 describes a method for culturing cells on surfaces. On page 4, lines 25-30 D3 describes that cellulose is epoxide activated when fibrous protein is bonded to cellulose. It is considered obvious to a person skilled in the art to combine D1 and D3 to achieve the invention according to claims 12-14, 17, 18. Therefore, claims 12-14, 17, 18 are not considered to involve an inventive step.

To use nucleotides coupled to microcarriers is known, see D4 page 1, part 2, page 4, part 29. It is considered obvious to a person skilled in the art to combine what is known from D1, D3 and D4 to achieve the invention according to claim 16. Hence, the claimed invention according to claim 16 is not considered to involve an inventive step.

Documents D5-D7 merely describe the state of the art and are not commented on further.

Accordingly, claims 1-6, 9-14, 16-30 are not considered to involve an inventive step.

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/001414

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 18 does not meet the requirements of Article 6 PCT because it refers both to method claims, claims 12-17, and product claims, claims 1-10.